Summary
Natural products have been the source of most of the active ingredients of medicines. The use of natural products, with therapeutic properties is as ancient as human civilization. Since from long time, the minerals, plants and animals products were the main sources of drugs. The industrial revolution and the development of organic chemistry, resulted in a preference for synthetic products for pharmacological treatment. The reasons for this were that the pure compounds were easily obtained, structural modifications to produce potentially more active and safer drugs could be easily performed and the economic power of the pharmaceutical companies was increasing. Furthermore, throughout the development of human culture, the use of natural products has had magical-religious significance. The plants are naturally gifted for the synthesis of medicinal compounds, whose characterization has led to the discovery of new drugs, with high therapeutic potentials. Euphorbiaceae is one among the large flowering plant families, consisting of a wide variety of vegetative forms, some of which are plants of great importance in medicine. Its classification and chemistry have of late been subjects of interest, possibly because of the wide variety of chemical composition of its members.

The plant *Epiprinus mallotiformis* belongs to the family Euphorbiaceae, distributed throughout the Western Ghats (evergreen rain forest region) of Karnataka. Gowda (2004) documented the traditional uses of the plant *E. mallotiformis* in his book ‘Vanaspathi Kosha’ used to treat various human ailments viz., diuretic problems, digestive problems, dysentery, external wounds, microbial infections etc. Further, it is used as laxative, remedy for vesicle calculi, ulcers, gonorrhea etc. Literature survey indicated that, *E. mallotiformis* is unique medicinal plant in the Western Ghats and it has
not been studied comprehensively. Hence, the studies on phytochemical and pharmacological properties of *E. mallotiformis* have been carried out.

The leaf and bark Sample of *Epiprinus mallotiformis* were collected from the Agumbe region of Shimoga district, Karnataka, India. The leaf and bark samples were shade dried and mechanically powdered. The powdered materials were subjected to Soxhlet extraction by successively, with low polar to high polar organic solvents, such as petroleum ether, chloroform, methanol and water. The obtained extracts were concentrated to dryness in a rotary flash evaporator. The highest yield was obtained in the methanol followed by aqueous, chloroform and petroleum ether. In general, the total yield of extracts, obtained from leaves was found to be more, when compare to bark. The concentrated extracts were subjected to qualitative phytochemical analysis. The Leaf and bark extracts showed the presence of flavonoids, glycosides, saponin, steroids and tannins.

Methanolic leaf extract was selected and subjected for isolation and characterization of bioactive compounds, by employing column chromatography and possible chemical structures were elucidated by IR, $^1$HNMR, $^{13}$CNR and mass spectral studies. The characterized compounds were found to be Hesperidin, Apigenin-7-glycosides, Aliphatic tetrol and 13-labdene-2,3,8,15-tetrol.

Determination of nutritive value *viz.*, ash, crude protein, moisture, crude fat, crude fiber and carbohydrate, macro and micro elemental composition of both young and mature leaves of *E. mallotiformis*, evaluated. The results showed that, the leaves are rich in carbohydrate and crude protein contents and they also show high level of moisture, fiber and ash values. However, the young leaves are rich in macro nutrients, whereas,
mature leaves are rich in micro nutrients. But, the overall nutritive value of young and mature leaves was found to be more or less similar. Among the macronutrients, Ca is dominant, which was followed by Mg, N, K and P. In case of micronutrients, Mn was dominant followed by Fe, Zn and Cu in both young and matured leaf samples.

Pharmacological experiments were designed to screen antimicrobial activity, antioxidant activity, hepatoprotective activity, wound healing activity, analgesic activity, anti-inflammatory activity and anthelmintic activity of *E. mallotiformis*.

Antimicrobial activity of the leaf and bark extracts and 13-labdene-2,3,8,15-tetrol of *E. mallotiformis* was tested against some human pathogenic gram positive, gram negative bacteria and pathogenic fungi. Antimicrobial activity was performed through agar well diffusion method. Among the leaf and bark extracts, methanolic leaf extract showed the significant activity. The isolated pure compound (13-labdene-2,3,8,15-tetrol) showed comparable antimicrobial activity, when comparable with the leaf methanolic extract. The results of antibacterial activity showed that, maximum inhibition found in *Escherichia coli*, followed by *Klebsiella pneumonia*, *Pseudomonas aeruginosa* and *Salmonella typhi*. Among test fungi, greater inhibition found in *Microsporum gypseum*, *Trichophyton rubrum*, *Chrysosporium merdarium* and *C. keratinophilum* against all the extracts as well as pure compound, 13-labdene-2,3,8,15-tetrol.

*In vitro* antioxidant activities was studied for the leaf and bark extracts and isolated pure compound, 13-labdene-2,3,8,15-tetrol of *E. mallotiformis* viz., DPPH radical scavenger activity, metal chelating activity, hydrogen peroxide scavenging activity and total reductive capability. The maximum antioxidant activity was found in leaf methanolic extracts compared to bark extracts. Whereas, isolated pure compound
showed significant activity at increased concentrations in all the different antioxidant assays.

For animal experiments, the LD$_{50}$ value obtained from methanolic leaf and bark extracts and isolated pure compound, 13-labdone-2,3,8,15-tetrol was 3000 mg/kg body weight. Therefore, $1/10^{th}$ weight of maximum tolerated dose were found to be 300 mg/kg body weight of leaf and bark extracts and isolated pure compound, 13-labdone-2,3,8,15-tetrol. However, 100mg/kg, 200 mg/kg and 300 mg/kg body weight were chosen for the study.

In-vivo antioxidant assays performed to do estimation of catalase enzyme (CAT) activity, estimation of super oxide dismutase enzyme activity (SOD), estimation of peroxidase enzyme activity and estimation of lipid peroxidation. Pretreatment of rats with suspension of methanolic leaf and bark extracts and isolated pure compound, 13-labdone-2,3,8,15-tetrol of *E. malloiformis* at 100mg/kg, improved the enzyme level and preserved catalase, SOD, peroxidase and lipid peroxidation activates compared to control and CCl$_4$ groups.

Hepatoprotective activity was carried out for methanolic leaf and bark extracts and 13-labdone-2,3,8,15-tetrol. Blood serum analysis was carried out to estimate the liver function markers *viz.*, Serum glutamate pyruvate transaminases (SGPT), serum glutamate oxaloacetate transaminases (SGOT) and alkaline phosphatases value (ALP) on CCl$_4$ intoxicated rats. Intoxication of rats with carbon tetrachloride significantly altered the biochemical parameters, when compared with normal control rats. In the carbon tetrachloride treated group of animals, serum SGOT, SGPT and ALP levels were significantly elevated. Animal groups treated with methanolic leaf and bark extracts and
isolated pure compound, 13-labdon-2,3,8,15-tetrol of \textit{E. mallotiformis} showed significant decrease in serum levels of SGOT, SGPT and ALP at 100 mg/kg, when compared with CCl\textsubscript{4} treated rats. Standard drug silymarin also exhibited similar results significantly.

The histopathological observations basically support the results obtained from serum enzyme assays. Histology of the liver section of normal control animals, showed normal hepatic cells, with well-preserved normal lobular pattern, while significant hepatoprotective activity was observed in all the test animals treated with methanolic leaf and bark extracts and isolated pure compound, 13-labdon-2,3,8,15-tetrol, similar to the standard drug silymarin treated animals.

Wound healing activity was carried out for methanolic leaf and bark extracts and 13-labdone-2,3,8,15-tetrol using three different animal models, such as, excision wound, incision wound, dead space method. In all the three models, methanolic leaf extract and isolated pure compound, 13-labdone-2,3,8,15-tetrol exhibited significant activity at 300 mg/kg concentration by wound contraction in excision wound model, whereas, increased tensile breaking strength was recorded in incision wound model and increased dry weight of granulation tissue was observed in dead space wound model. The granulation tissue of 300 mg/kg methanolic extract treated animal group showed less number of necrotic cells, with significant epithelialization, improved rate of collagen formation, decreased accumulation of macrophages at the site of injury, when compare to the control group of animals.

Analgesic activity was carried out for methanolic leaf and bark extracts and 13-labdone-2,3,8,15-tetrol, using three different animal models, such as, abdominal writhing method, tail flick method and hot plate method. In all the three models, the
result obtained in analgesic activity was found to be dose dependent. The methanolic leaf extract and isolated pure compound, 13-labdone-2,3,8,15-tetrol, exhibited significant activity at higher concentration (300 mg/kg).

Anti-inflammatory activity was carried out for methanolic leaf and bark extracts and 13-labdone-2,3,8,15-tetrol. It is performed by carrageenan induced paw edema. Carrageenan-induced inflammation in rats paw represents a classical model of edema formation and hyperalgesia, which has been extensively used in the development of nonsteroidal anti-inflammatory drugs. The results obtained in anti-inflammatory activity were found to vary according to dose dependent manner. The methanolic leaf extract and isolated pure compound, 13-labdone-2,3,8,15-tetrol exhibited significant anti-inflammatory activity at higher concentration (300 mg/kg).

*In vitro* anthelmintic activity was carried out for of the leaf and bark extracts and 13-labdone-2,3,8,15-tetrol. Indian adult earthworms (*Pheretima posthuma*) were selected for *in vitro* anthelmintic assay. It has anatomical and physiological resemblance with the intestinal round worm parasites of human beings. The results obtained in anthelmintic activity experiments were found to be dose dependent. The methanolic leaf extract and 13-labdone-2,3,8,15-tetrol showed considerable anthelmintic activity (paralysis and death time) at higher concentration (100 mg/ml), whereas, bark extracts showed low anthelmintic activity over the leaf methanolic extracts, isolated pure compound and standard drug.

In general, the methanolic leaf extract and isolated pure compound, 13-labdone-2,3,8,15-tetrol showed considerable anthelmintic activity at higher concentration i.e., at 100 mg/ml, over the standard drug, piperazine citrate at 10 mg/ml concentration.